REMARKS

Applicants appreciate the thorough examination of the present application as evidenced by the Office Action dated November 9, 2006. Claims 1-9 and 21 are pending in this application. Claims 3, 6-9 are currently withdrawn from the consideration as directed to non-elected species. Claims 1-2, 4-5 and 21 are currently under the examination. Claims 1-2, 4-5 and 21 are rejected under 35 U.S.C. § 102 (b) as being anticipated by or alternatively under 35 U.S.C. § 103(a) as being obvious over Lowden CT, Antiviral Acridones, *Dissertation Abstracts International*, Vol. **3B**, P 1398 (2001) (Hereinafter the "Lowden dissertation publication"). Applicants hereby request further consideration of the application in view of the comments that follow.

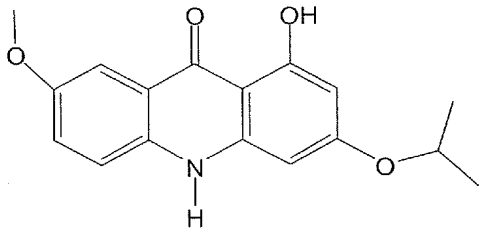
I. New Claim 22

Applicants have added new Claim 22 directed to a method of claim 1, wherein said virus is human cytomegalovirus; and said compound is 3-allyloxy-1-hydroxy-7-methoxyacridone or a pharmaceutically acceptable salt thereof.

Claim 22 is supported by the specification, for example, at page 19, lines 16-19 and compound 10. The new claim 22 presents no new matter and is supported by the specification as originally filed, and Applicants respectfully request entry thereof.

II. § 102(b) rejections of Claims 1-2, 4, 5 and 21

Claims 1-2, 4, 5 and 21 stand rejected under 35 U.S.C. § 102(b) as being anticipated by the Lowden dissertation publication. The species elected for the examination is 1-hydroxy-3-isopropoxy-7-methoxyacridone (compound 8 in the present application and ***compound 38*** in the Lowden dissertation publication). (*See* below structure of compound 38.) Applicants respectfully disagree with this assertion and reconsideration is respectfully requested.

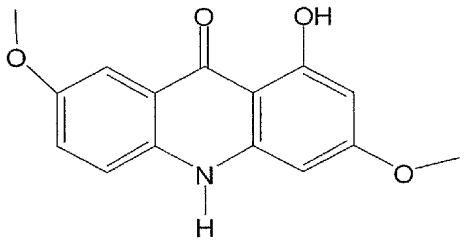


Compound 38: 1-hydroxy-3-isopropoxy-7-methoxyacridone

Anticipation under 35 U.S.C. § 102 requires that each and every recitation of the claim be found in a single prior art reference. *W. L. Gore & Associates Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1554, 220 U.S.P.Q. 303, 313 (Fed. Cir. 1983). A finding of anticipation further requires that there must be no difference between the claimed invention and the disclosure of the cited reference as viewed by one of ordinary skill in the art. *See Scripps Clinic & Research Foundation v. Genentech Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991).

It is the Examiner's position that, in light of the teachings of the Lowden dissertation publication which states that the plaque assay is the accepted standard approach for measuring anti HCMV activity and that a number of acridone derivatives exhibit in vitro activity, one of ordinary skill in the art would reasonably anticipate that 1-hydroxy-3-isopropoxy-7-methoxyacridin-9 (10H)-one (compound 8 in the present application and ***compound 38*** in the Lowden dissertation publication) would be effective in treating subjects infected with HCMV wherein the method comprises administering compound 38. (*See* Action, page 3.) Applicants respectfully disagree with Examiner's assertion.

The Lowden dissertation publication describes that 1-hydroxyl-3, 7-dimethoxyl acridin-9 (10H)-one (***compound 4*** in the Lowden dissertation publication) (*see* bellow structure of compound 4), ***rather than*** the elected species ***compound 38***, might be a possible lead compound of HCMV because compound 4 shows a preliminary anti-HCMV activity in the plaque assay.



Compound 4:1-hydroxyl-3, 7-dimethoxyl acridin-9 (10H)-one

The Lowden dissertation publication merely suggests that compound 38 was evaluated at a very preliminary stage by the plaque assay, and no other biological assay was conducted for ***compound 38***. In light of the limited biological data of the analogs of compound 4, the Lowden dissertation publication has conceded that only very limited conclusions can be drawn regarding the Structure Activity Relationship (SAR) of the HCMV analogs, and a more comprehensive biological evaluation must be completed. (*See,* the Lowden dissertation publication, page 88, lines 1-2 and page 131, lines 14-15.) Regarding the plaque assay, the Lowden dissertation publication kept emphasizing that although the plaque assay is the accepted standard approach for measuring anti-HCMV activity, it is time-consuming, difficult to reproduce and variable in practice, and, because of these disadvantages, very few analogs have been evaluated for HCMV inhibitory activity. (*See*, the Lowden dissertation publication, page 131, lines 15-20.) Therefore, contrary to the Examiner's assertion, in the Lowden dissertation publication, the elected species, compound 38 was merely identified as a HCMV biologically active compound without any other biological activity data such as selectivity data, and the plaque assay is a biological assay which can only provide a preliminary determination of the activity. Therefore, in view of the limited in vitro data in the Lowden dissertation publication of compound 38 and the incomplete biological assay, one of ordinary skill in the art would not anticipate that compound 38, can be used to develop a method of treating beta-herpes virus infection.

Therefore, the Lowden dissertation publication is not qualified as a § 102 references because it fails to disclose each and every recitation of the claim. Accordingly, Applicants submit that Claims 1-2, 4, 5 and 21 are not anticipated by the Lowden dissertation publication and respectfully request that these rejections be withdrawn.

III. § 103(a) rejections of Claims 1-2, 4, 5 and 21

Claims 1-2, 4, 5 and 21 stand rejected under 35 U.S.C. § 103(a) as being obvious over the Lowden dissertation publication. Applicants respectfully disagree with this assertion and reconsideration is respectfully requested.

The Examiner has asserted that the Lowden dissertation publication teaches an in vitro method of inhibiting HCMV replication by reducing HCMV plaque formation in human embryonic (HEL) cells infected with HCMV and the method comprises administering the compound 1-hydroxy-isopropoxy-7-methoxylacridin-9 (10H)-one (***compound 38***) to HCMV infected HEL cells. (*See* Action, pages 4-5.) The Examiner has conceded that the cited reference does not explicitly teach an in vivo method of treating an HCMV infected subject by inhibiting HCMV replication which comprises administering compound 38 to a HCMV infected subject as recited in Claim 1. (*See* Action, page 5.) The Examiner, however, has stated that one of ordinary skill in the art would be motivated to conduct in vivo scientific experiments which comprises administering compound 38 to HMCV infected subject and reach the present invention. (*See* Action, page 7.) Applicants respectfully disagree with the Examiner's assertion.

Three basic criteria must be met in order to establish a prima facie case of obviousness. 1) The prior art must teach or suggest all the claim recitations. *See In re Wilson*, 57 C.C.P.A. 1029, 1032 (C.C.P.A., 1970). 2) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine references teachings in order to achieve the claimed invention. *See In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788; 1790 (Bd. Pat. App. & Int. 1986). 3) There must be a reasonable expectation of success. See M.P.E.P. § 2143. Further, it is the burden of the Examiner to establish a prima face case of obviousness. *See In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir., 1984).

The Lowden dissertation publication merely suggests a starting point of developing a treatment for HCMV infection by using ***compound 4 rather than compound 38*** as a possible lead compound. As it is known to one of ordinary skill in the art, the identification of a lead

compound is only the first step of developing a possible pharmaceutical treatment. A series of studies such as lead optimization, SAR study and selectivity study, etc, are required to complete before conducting in vivo experiments. In the Lowden dissertation publication, neither lead optimization study nor compounds' selectivity study were conducted. The data in the Lowden dissertation publication only shows ED_{50} and IC_{50} data of compound 4 and some analogs of compound 4 (including compound 38) are active but with no further biological activity data. In light of the limited biological activity data of compound 38, very limited conclusions can be drawn regarding the biological activity of compound 38. In addition, regarding the plaque assay, as discussed above, the plaque assay is only a preliminary test of determining a compound's HCMV activity and it is not able to measure the accurate biological activity of the compound. Thus, the plaque assay does not provide a complete set of in vitro data for developing a method of treatment by administering compound 38. Thus, in view of the in vitro data provided in the cited reference, Applicants submit that the Lowden dissertation publication does not teach or suggest a method of treatment of beta Herpes virus infection by administering the compound 1-hydroxy-isopropoxy-7-methoxylacridin-9 (10H)-one (***compound 38***) either in vitro or in vivo.

Furthermore, there is no reasonable expectation that the development of the method of treating beta Herpes Virus infection would be successful. As one of ordinary skill in the art knows after a lead compound is identified, it still requires endless experiments to optimize the lead compound such as extensive SAR study and conducting selectivity study to get to the point that the chance of successfully developing a method of treatment is reasonable. The Federal Circuit stated that a prior art suggesting virtually endless experimentation is not a case of prima facie obviousness. *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ 2d 1529, 1532 (Fed. Cir. 1989). Considering the limited biological activity data of compound 38 in the Lowden dissertation publication, the possibility of successfully developing a method of treating beta Herpes virus infection by administering compound 38 is so slim that it is analogous to looking for a needle in a hay stack, which is not prima facie obviousness. Thus, the teachings of the Lowden dissertation publication would not provide a reasonable

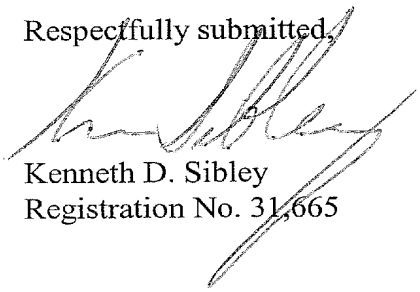
expectation of success to one of ordinary skill in the art to modify the cited references to reach the present invention, which is legally required to maintain the outstanding rejection.

In view of the foregoing, Applicants respectfully submit that the claimed subject matter is nonobvious over the Lowden dissertation publication, and that the rejection cannot be maintained. Accordingly, Applicants request that the rejection under § 103(a) be withdrawn.

CONCLUSION

Accordingly, Applicants submit that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any small matters outstanding of resolution, he is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

Respectfully submitted,



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